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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/760,557	01/21/2004	Wolf-Georg Forssmann	P60448US1	8650

136 7590 05/26/2006

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EXAMINER

MERTZ, PREMA MARIA

ART UNIT	PAPER NUMBER
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1646

DATE MAILED: 05/26/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/760,557	Applicant(s) FORSSMANN ET AL.	
	Examiner Prema M. Mertz	Art Unit 1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 April 2006.
 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 9-19 is/are pending in the application.
 4a) Of the above claim(s) 10-12, 14-15, 18-19 is/are withdrawn from consideration.
 5) ☐ Claim(s) _____ is/are allowed.
 6) ☒ Claim(s) 9, 13, 16 and 17 is/are rejected.
 7) ☐ Claim(s) _____ is/are objected to.
 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) ☐ All b) ☐ Some * c) ☐ None of:
 1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
 * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>1/21/2004</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION***Election/Restrictions***

1. Applicant's election with traverse of Group I, claims 9, 13, 16, 17 (4/14/06) is acknowledged. The traversal is on the ground(s) that the restriction is improper since the examiner has not shown that examination of the polypeptides of SEQ ID NO: 6 and modified SEQ ID NO:6 would be a burden because all of the amino acids sequences share a substantial structural feature, i.e. the basic sequence of amino acid residues found in SEQ ID NO:6. This argument is not found persuasive because the searches for the protein and its variant would not overlap. The inventions listed in the different Groups do not relate to a single general inventive concept because they lack the same or corresponding special technical features for the following reasons. With respect to the elected peptide of amino acid sequence set forth in SEQ ID NO:6, the special technical feature of the invention encompassing the peptide of SEQ ID NO:6 is the amino acid sequence of SEQ ID NO:6. The other peptide listed does not share the special technical feature (SEQ ID NO:6) because the other peptide is a structurally different N-terminal variant of SEQ ID NO:6. The test for propriety of restriction is not whether the inventions are related but rather whether they are distinct and whether it would impose a burden on the examiner to search and examine multiple inventions in a single invention. The two different peptides are independent and distinct, each from the other, which possess characteristic differences in structure that is distinct for each invention which cannot be exchanged.

Lastly the inventions are distinct because a search of the literature for the peptide of SEQ ID NO:6, would not be expected to reveal art for the other peptide with the N-terminal

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truncation, which searches are extensive requiring separate searches, which would be unduly burdensome.

Having shown that these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different and recognized divergent subject matter as defined by MPEP. § 808.02, the Examiner has *prima facie* shown a serious burden of search (see MPEP. § 803). Therefore, an initial requirement of restriction for examination purposes as indicated is proper.

The Groups as delineated in the restriction requirement (2/16/06) are patentably distinct one from the other such that each invention could, by itself, in principle, support its own separate patent (as shown by the arguments put forth in the written restriction requirement).

The requirement is still deemed proper and is therefore made FINAL.

Claims 10-12, 14-15, 18-19 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Specification

2. The disclosure is objected to because of the following informalities:

There is no title "Brief description of the Drawings", and no description of each of the Figures, which is required as set forth in 37 C.F.R. § 1.74. Appropriate correction is requested.

3. It is clear from the declaration that Applicants intend to claim priority to the earlier filed applications. If applicant desires priority under 35 U.S.C. 120 based upon a previously filed copending application, in this case the instant application is a 371 of PCT/EP94/04282, specific reference to the earlier filed applications must be made in the instant application as "Cross Reference to Related Application". This should appear as the first sentence of the specification

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following the title, preferably as a separate paragraph. The status of non-provisional application(s) (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression "now Patent No. _____" should follow the filing date of the parent application. If a parent application has become abandoned, the expression "now abandoned" should follow the filing date of the parent application.

In the instant case, in the specification below the title, Applicants should insert between lines 2 and 3,

--"Cross Reference to Related Application"

This Application is a continuation of 08/666,340, filed 08/18/1998, now abandoned, which is a 371 of PCT/EP94/04282 filed 12/22/94.--

Claim objections

4. Claim 16 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 17.

When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC § 101

5. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 9, 13, 16-17 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

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The claims are directed to cytokine polypeptide, CC-1, 74 amino acids in length. The invention encompassed by these claims has no apparent or disclosed patentable utility. This rejection is consistent with the current utility guidelines, published on 1/5/01, 66 FR 1092. The instant application has provided a description of an isolated protein, but does not disclose a specific and substantial biological role of this protein or its significance. There is no biological activity, phenotype, disease or condition, or any other specific feature that is disclosed as being associated with the CC-1 polypeptide. The specification (page 3, third paragraph) states that “the biological activity is that of a cytokine” and that (page 6, last paragraph; page 7, first 2 lines):

“A data bank comparison was performed on Swiss-Prot and EMBL-Peptid and Nukleinsäuredatenbank. A sequence homology was established to various members of the superfamily of intercrines with a maximum homology to macrophage inflammatory protein MIP I alpha and MIP I beta.”.

However, no comparison or degree of homology with the instant CC-1 protein and any of the other intercrines has been provided in the instant specification as filed. The mere identification of the CC-1 polypeptide is not sufficient to impart any particular utility to the claimed polypeptide without any information as to the specific properties of CC-1. Since significant further research would be required of a person skilled in the art to determine how the claimed polypeptide is involved in any activities, the asserted utilities are not substantial.

The assertion that the disclosed CC-1 protein has cytokine activities cannot be accepted in the absence of supporting evidence, because there are cytokines that are members of families wherein individual members have distinct and sometimes even opposite, biological activities. Cytokine or growth factor polypeptide families are known in the art to have different biological

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activities, despite a close structural relationship. For example, Tischer et al. (U.S. Patent 5,194,596) establishes that VEGF (a member of the PDGF, or platelet-derived growth factor, family) is mitogenic for vascular endothelial cells but not for vascular smooth muscle cells, which is opposite to the mitogenic activity of naturally occurring PDGF which is mitogenic for vascular smooth muscle cells but not for vascular endothelial cells (column 2, line 46 to column 3, line 2). The differences between PDGF and VEGF are also seen in vivo, wherein endothelial-pericyte associations in the eye are disrupted by intraocular administration of PDGF but accelerated by intraocular administration of VEGF (Benjamin et al., 1998, Development 125:1591-1598, see Abstract and pp. 1594-1596).

In the transforming growth factor (TGF) family, Vukicevic et al. (1996, PNAS USA 93:9021-9026) disclose that OP-1, a member of the TGF- β family of proteins, has the ability to induce metanephrogenesis, whereas closely related TGF- β family members BMP-2 and TGF- β 1 had no effect on metanephrogenesis under identical conditions (p. 9023, paragraph bridging columns 1-2).

Generally, the art acknowledges that function cannot be predicted based solely on structural similarity to a protein found in the sequence databases. For example, Skolnick et al. (2000, Trends in Biotech. 18:34-39) state that knowing the protein structure by itself is insufficient to annotate a number of functional classes, and is also insufficient for annotating the specific details of protein function (see Box 2, p. 36).

Therefore, based on the discussions above concerning the specific examples of structurally similar proteins that have different functions, along with the art's recognition that one cannot rely upon structural similarity alone to determine functionality for new members of

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cytokine or growth factor polypeptide families, the assertion that the CC-1 polypeptide recited in the claims has cytokine biological activities is not specific or substantial. Significant further research would have been required of the skilled artisan to characterize the polypeptide of SEQ ID NO: 6 to determine its particular biological activities or other specific utilities.

In view of the evidence in the art that structural similarity between soluble polypeptides like interleukins, as well as other cytokines and growth factors, cannot accurately predict functional similarity, there is also no well-established utility for the CC-1 protein. Furthermore, since the asserted utility is not present in a ready-to-use, real-world application, the asserted utility is not substantial.

The specification asserts several utilities for the polypeptide of SEQ ID NO:6, that are not necessarily related to its biological activities; however, none of these asserted utilities meets the three-pronged test of being credible, specific and substantial. Each will be addressed in turn:

1. *as a diagnostic agent.* This asserted utility is not specific or substantial. Since antibodies can be made to any polypeptide, the asserted utility is not specific to the CC-1 polypeptide. Furthermore, the specification does not disclose how anti-CC-1 antibodies can be used and for diagnosis of what conditions. Therefore further significant research would be required on one skilled in the art to determine how to use antibodies to the claimed CC-1 polypeptide. Since the asserted utility is not presented in a ready-to-use, real-world application, the asserted utility is not substantial.

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2. *to produce derivates to be employed as hybridization probes.* This asserted utility for the polynucleotide encoding the CC-1 polypeptide is not specific or substantial. Since hybridization assays can be performed with any polynucleotide, the asserted utility is not specific to the claimed polypeptide (SEQ ID NO:6). Also, since the specification does not disclose how the variants of the polypeptide or polynucleotide encoding said polypeptide, can be used, significant further research would be required of a person skilled in the art to determine how to use the claimed variants. Since the asserted utility is not present in a ready-to-use, real-world application, the asserted utility is not substantial.

3. *as a medicament.* This asserted utility is not specific or substantial. The specification on page 3, third paragraph, lines 1-2, discloses that:

“The peptide according to the invention may be used as a medicament.”

The specification alleges that the CC-1 polypeptide can be employed as a medicament for treating diseases, for example, of the immune system. Diseases of the immune system encompass AIDS, infections and cancer. However, the specification does not disclose the role of the CC-1 protein in the immune system i.e. is a proinflammatory or an anti-inflammatory cytokine. The specification does not disclose any specific diseases or disorders associated with CC-1. Furthermore, since many proteins can and are used as therapeutic reagents, the asserted utility is not specific to the claimed CC-1 polypeptide. Since the asserted utility is not presented in a ready-to-use, real-world application, the asserted utility is not substantial.

Claim rejections-35 USC § 112, first paragraph

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6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 9, 13, 16-17 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a substantially asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. The instant specification does not disclose a biological activity for the claimed CC-1 protein, therefore, there is no specific and substantial asserted utility or well established for the claimed CC-1 protein.

Claim rejections-35 USC § 112, first paragraph, scope of enablement

7. Claims 9, 13, 16-17, are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated, chemically synthesized, or recombinantly produced cytokine polypeptide selected from the group consisting of: (a) the polypeptide of amino acid sequence set forth in SEQ ID NO:6, does not reasonably provide enablement for a cytokine as recited in claim 9. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification is not enabling for "the amino acid sequence modified by amidization, acetylation, phosphorylation, and/or glycosylation exhibiting cytokine biological activity" as recited in claim 9(b) because the specification only enables a cytokine CC-1 of amino acid

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sequence shown in SEQ ID NO:6, the polypeptide having specific characteristics. The term “modified” without the recitation of an amino acid sequence encompasses amino acid sequences that can deviate from the amino acid sequence shown in SEQ ID NO:6, therefore, different proteins with different amino acid sequences would be encompassed by the claim. Furthermore, even if the amino acid sequence was recited in the claim, the specification is nonenabling for a cytokine as recited in claim 9(b), in which a cytokine is modified by amidization, acetylation, phosphorylation, and/or glycosylation exhibiting cytokine biological activity, because the specification fails to recite a cytokine with these features. In the absence of this information a practitioner would have to resort to a substantial amount of undue experimentation before they could even begin to rationally design a CC-1 polypeptide having other than a natural amino acid sequence. The disclosure of a single natural amino acid sequence is clearly insufficient support under the first paragraph of 35 U.S.C. § 112 for claims which encompass any and all derivatives of CC-1, including mutants thereof.

Claim rejections, 35 U.S.C. § 112, second paragraph

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 9, 13, 16-17 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 9 is rejected for several reasons.

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Claim 9, line 3, is vague and indefinite because it recites “cytokine biological activity”. The metes and bounds of this term are unclear. Which cytokine activity is being referred to in the claims? Is it pro-inflammatory or anti-inflammatory activity?

Claim 9 is vague and indefinite because it recites “...amino acid sequence SEQ ID NO:6”. It is unclear whether this recitation is open or closed language. It is suggested that the claim be amended to recite “consists of the amino acid sequence set forth in SEQ ID NO:6”. Claims 9(b) is vague and indefinite because it fails to recite the amino acid sequence of the protein that is modified.

Claim 17 is vague and indefinite because it recites “the recombinant cytokine SEQ ID NO:6 of claim 9”, which is a duplicate of claim 16 and it is unclear that the recitation of “SEQ ID NO:6” is the amino acid sequence of the cytokine. Furthermore, it is suggested that claim 17, be amended to recite “the recombinant cytokine of claim 9 said cytokine consisting of the amino acid sequence set forth in SEQ ID NO:6” because the amino acid sequence is a property of the protein. It is suggested that claim 16 be deleted and claim 9 be amended as suggested to obviate this rejection and the objection set forth in paragraph 4.

Claims 13 and 16 are rejected as vague and indefinite insofar as they depend on claim 9 for its limitations.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

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(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

9a. Claim 9, 13, 16-17, are rejected under 35 U.S.C. § 102(e) as being anticipated by Rosen et al. (U.S. Patent No. 5,556,767).

Rosen et al teach a chemokine macrophage inflammatory factor-1 γ (MIP-1 γ), disclose the nucleotide sequence of the polynucleotide and corresponding amino acid sequence of the chemokine, recombinant vectors comprising the polynucleotide, a recombinant host cell and a method for producing the chemokine polypeptide (see abstract; Figure 1; and Examples I-II, columns 12-14). Rosen teach the nucleotide sequence which encodes the amino acid sequence of the chemokine including the mature form of the MIP-1 γ , which may be in the form of a preprotein or prepolyptide which includes a leader or secretory sequence (column 4, lines 1-8), which may be naturally present on the chemokine and disclose the chemokine expression in mammalian COS cells (see column 13, lines 55-67; column 14, lines 1-49). Rosen et al also teach that the secreted protein (MIP-1 γ), without the signal sequence, obtained from the COS cell culture media was separated and analyzed on a 15% SDS-PAGE gel (see Figure 4). The MIP-1 γ polypeptide in a pharmaceutically acceptable buffer (see column 9, lines 23-30) meets the limitations of instant claim 13. The secreted MIP-1 γ polypeptide in the Rosen et al. reference, is the same as the polypeptide in SEQ ID NO:6 claimed in the instant application (see attached Sequence Comparison "A"). Therefore, the Rosen et al reference anticipates claims to cytokine CC-1 of SEQ ID NO:6

Applicants argue that Rosen discloses a polypeptide that is 93 amino acids long and does not suggest the 74-amino acid of the present claims. However, contrary to Applicants

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arguments, instant claim 9 recites “.....of amino acid sequence set forth in SEQ ID NO:6” and it is unclear whether this is open or closed language. Therefore, the protein disclosed in the Rosen reference meets the limitations of instant claims 9, 13, 16-17.

Conclusion

No claim is allowed.

Claims 9, 13, 16-17 are rejected.

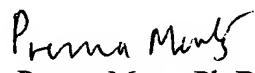
Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Prema Mertz whose telephone number is (571) 272-0876. The examiner can normally be reached on Monday-Friday from 7:00AM to 3:30PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, can be reached on (571) 272-0835.

Official papers filed by fax should be directed to (571) 273-8300. Faxed draft or informal communications with the examiner should be directed to (571) 273-0876.

Information regarding the status of an application may be obtained from the Patent application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


Prema Mertz Ph.D., J.D.
Primary Examiner
Art Unit 1646
May 8, 2006